UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,474	04/20/2004	Tianmin Zhu	AM101007	7099

25291 7590 01/05/2010

WYETH LLC
PATENT LAW GROUP
5 GIRALDA FARMS
MADISON, NJ 07940

EXAMINER	
PACKARD, BENJAMIN J	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
01/05/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,474	ZHU ET AL.	
	Examiner	Art Unit	
	Benjamin Packard	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,14-20,32-38,50-56,68-80 and 92-96* is/are allowed.

6)☒ Claim(s) *3-13,21-31,39-49,57-67 and 81-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1pg (10/20/09)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/20/09 has been entered.

Applicants' arguments, filed 10/20/09, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Election/Restrictions

Applicants requested clarification of Examiner's comment with regards to claim 1 in the Office Action dated Oct 16, 2008, specifically where examiner stated that the amended claim 1 was partially directed to species that were independent.

Examiner was simply responding to Applicants request that the linking claims (claims 9-67 and 74-96) be rejoined as requested in the response filed 06/05/08 (see pg 19 or 22). In response, Examiner noted there was a species election in the restriction/election dated 09/04/07, to which Applicants elected the compound of formula III, wherein R1 is methyl, R2 is -S-, R3 is -CH2- R4 is OR7, R7 is COR9, R8 is methyl,

and R9 is methyl. As such, Examiner was simply noting rejoinder was not granted and examination had not been expanded beyond the elected species.

Now having found the elected species allowable in light of Applicants arguments, as discussed below, Examiner has now extended examination "to the extent necessary" to determine the patentability of the Markush-type claim, which includes all the compounds of claims 1-2. Because the compounds appear to be allowable, the search is expanded to include all claimed methods.

All claims are now examined.

Claim Rejections - 35 USC § 112 – Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-13, 21-31, 39-49, 57-67, and 81-91 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for U-87 MG human glioblastoma, does not reasonably provide enablement for the broader treatment of "a pathological condition or disorder mediated in a mammal" or treatment via the broader genus of compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue

experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to treatment of pathological conditions, such as lung cancer, brain cancer, ischemic heart disease, resetenosis, inflammation, platelet aggregation, etc. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Greenwald (Advanced Drug Delivery Reviews), as cited by Applicants in the response filed 10/20/09, which Applicants assert teaches paclitaxel itself, in the paragraph spanning the two columns of page 223, a different PEG conjugate of molecular weight 5,000 of paclitaxel is reported to be equivalent to paclitaxel *in vitro* against P388 cells but non-efficacious *in vivo*.

2. The breadth of the claims

The claims are broad insofar as the conjugated polymer varies where n can be from 1-1000 at the broadest and the conjugated polymer has a molecular weight from about 4000 to about 6000 at the narrowest. Further, the disorders to be treated art broad insofar as they vary from lung cancer to HIV.

3. The amount of direction or guidance provided and the presence or

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

absence of working examples

The specification provides no direction or guidance for practicing the claimed invention in its "full scope". No reasonably specific guidance is provided concerning useful therapeutic protocols for effective in vivo treatment of the wide range of pathological conditions instantly claimed, other than where the conjugated compounds III and IV (17-dihydro-17-(1-iodoacetyl)-wormannin or 11-desacetyl-11-(1-iodoacetyl)-wormannin is conjugated with PEG-SH-5000, respectively) at pgs 30-31 and 35-38 of the instant specification) is used against human non-small cell lung cancer in vitro and U87MG glioblastoma in vivo. The latter is corroborated by the working examples.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of sufficient experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used to treat pathological conditions, specifically lung cancer, as inferred by the claims and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the claimed invention in its "full scope" a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success. Further, the unpredictability of the *in vitro-in vivo* relation raises doubts as to whether the suggested variation of the conjugated portion of the compounds will have the same

in vivo effect as the single length conjugated wortmannin tested.

Allowable Subject Matter

Claims 1-2, 14-20, 32-38, 50-56, 68-80, and 92-96 appear to be free of the prior art and are thus allowed, where the closest prior art is Creemer et al (5,480,906, see IDS dated 4/20/2004) in view of Gutman et al (Toxins and Signal Transduction, Published by CRC Press, 1997, pg 429) and Zhu et al (US 6,331,547), as discussed in the prior Office Action mailed 3/17/09. While adding PEG and its variations to active agents appears to be a well known mechanism of increasing the solubility of low-solubility active agent, Applicants present persuasive remarks while citing Hollerman (Drug Metab Dispos) where wortmannin has a sufficient water solubility to achieve at least 95% of the desired activity, i.e. inhibition of PI3K binding (see pg 6 of 15 in the response filed 10/20/09). As such, the skilled artisan would not be motivated to increase the solubility of the active agent, given the solubility appears to be sufficient without conjugation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-F 8-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612